

What is claimed is:

1. A polypeptide with increased stability, relative to its corresponding wild type protein, having at least one non-natural amino acid incorporated into a hydrophobic region of the wild type polypeptide, wherein the amino acid so replaced is leucine, isoleucine, or valine.
2. The polypeptide of claim 1, wherein the polypeptide is a protein.
3. The non-natural amino acid of claim 1, wherein the non-natural amino acid is different from its corresponding natural amino acid in side chain functionality.
4. The polypeptide of claim 1, wherein the non-natural amino acid is a hydrophobic amino acid selected from the group consisting of an unsaturated hydrophobic amino acid; a fluorinated hydrophobic amino acid; 2-amino-3-methyl-4-pentenoic acid; 5,5,5-trifluoroleucine; 5,5,5,5',5'-hexafluoroleucine; 2-amino-3,3,3-trifluoro-methylpentanoic acid; 2-amino-3-methyl-5,5,5-trifluoropentanoic acid; 2-amino-3-methyl-4-pentenoic acid; 4,4,4-trifluorovaline; 4,4,4,4',4'-hexafluorovalin; homoallylglycine; homoproparglycine; and p-fluorophenylalanine.
5. A method for increasing stability of a polypeptide comprising introducing at least one non-natural amino acid into the hydrophobic region of the polypeptide thereby producing a polypeptide with increased stability relative to its corresponding wild type polypeptide.
6. The method of claim 5, wherein introducing the non-natural amino acid into the polypeptide involves replacing an existing, naturally occurring amino acid with a non-natural amino acid.

7. The method of claim 5, wherein introducing the non-natural amino acid into the polypeptide involves adding the non-natural amino acid into the polypeptide.
8. The method claim of 5, wherein the natural amino acid is a hydrophobic amino acid and the non-natural amino acid is a hydrophobic amino acid having side chain functionalities different from its corresponding natural amino acid.
9. The. method of claim 5, wherein the natural amino acid so replaced is leucine, and the non-natural amino acid is 5,5,5-trifluoroleucine.
10. The method of claim 5, wherein the naturally occurring amino acid so replaced is leucine, and the non-natural amino acid is 5,5,5,5',5',5'-hexafluoroleucine.
11. The method of claim 5, wherein the naturally occurring amino acid so replaced is leucine, and the non-natural amino acid is 2-amino-4-methyl-4-pentenoic acid.
12. The method of claim 5, wherein the naturally occurring amino acid so replaced is isoleucine, and the non-natural amino acid is selected from the group consisting of 2-amino-3,3,3-trifluoro-methylpentanoic acid; 2-amino-3-methyl-5,5,5-trifluoropentanoic acid; and 2-amino-3-methyl-4-pentenoic acid.
13. The method of claim 5, wherein the naturally occurring amino acid so replaced is methionine, and the non-natural amino acid is homoallyglycine or homoproparglycine.
14. The method of claim 5, wherein the natural amino acid is phenylalanine and the non-natural amino acid is p-fluoro-phenylalanine.